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(54) Title: MULTILAYER NONWOVEN TISSUE CONTAINING A SURFACE LAYER COMPRISING AT LEAST ONE HYALURONIC ACID ESTER		
(57) Abstract Provided is a multilayer nonwoven material, comprising a surface layer which comes into contact with the skin, and one or more other layers which do not come into contact with the skin, wherein said surface layer which comes into contact with the skin is a member selected from the group consisting of a surface layer comprising at least one derivative of hyaluronic acid, a surface layer comprising a mixture of said at least one derivative of hyaluronic acid and at least one natural polymer, semisynthetic polymer, or synthetic polymer, and a surface layer comprising a natural, synthetic, or semisynthetic biocompatible perforated membrane compatible with cell growth on its surface. The derivative of hyaluronic acid can be a hyaluronic acid ester. This material can be employed in a wide variety of medical and sanitary applications, including surgery and as a non-adhesive covering material.		

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MULTILAYER NONWOVEN TISSUE CONTAINING A SURFACE LAYER
COMPRISING AT LEAST ONE HYALURONIC ACID ESTER

BACKGROUND OF THE INVENTION

Field of the Invention

5 The present invention relates to a new material,
i.e., a multilayer nonwoven tissue, wherein one of the
layers comprises a hyaluronic acid derivative.

Description of Related Art

10 Studies aimed at obtaining biomaterials composed of
hyaluronic acid esters used as such or in mixtures with
other polymers, which provide good skin coverage, have
led to the creation of various types of products.
Tissues such as the gauzes and films described in U.S.
Patents Nos. 4,851,521 and 4,965,353 have been proposed.
15 Limitations on the use of such products as skin
coverings are due to their degree of rigidity, which may
vary according to how they are made, and to their poor
absorption of fluids, such as those exuding from wounds
during tissue repair. By using nonwoven tissue
20 production techniques, it is possible to obtain products
which combine flexibility with the capacity to strongly
absorb fluids. These characteristics are described in
various patents, such as U.S. Patent 5,041,104.

25 Limitations on the use of products composed of
hyaluronic acid derivatives and/or their mixtures,
obtained using currently known techniques, can for the

most part be attributed to:

(1) the poor mechanical characteristics of the material when wet, due to its tendency to form a gel when it comes into contact with aqueous fluids such as physiological fluids;

(2) the excessive use of expensive materials such as hyaluronic acid derivatives or mixtures thereof with other biocompatible and bioabsorbable polymers, resulting in a high cost of the finished product, despite the fact that the polymer need only be present in the layer directly in contact with the application site; and

(3) excessively high vapour transmission values.

These drawbacks are particularly significant in cases where poor exudate production is present.

SUMMARY OF THE INVENTION

Accordingly, an object of the present invention is to provide a multilayer nonwoven material, comprising a surface layer which comes into contact with the skin, and one or more other layers which do not come into contact with the skin, wherein said surface layer which comes into contact with the skin is a member selected from the group consisting of a surface layer comprising at least one derivative of hyaluronic acid, a surface layer comprising a mixture of said at least one derivative of hyaluronic acid and at least one natural polymer, semisynthetic polymer, or synthetic polymer, and a surface layer comprising a natural, synthetic, or semisynthetic biocompatible perforated membrane compatible with cell growth on its surface. In a preferred embodiment, the layer which contacts the skin comprises a hyaluronic acid derivative, i.e., a compound containing a hyaluronic acid moiety, especially a hyaluronic acid ester or mixtures thereof.

Such products possess good mechanical and fluid absorption characteristics, are flexible and soft,

reasonably priced, and can be varied with respect to their permeability to water vapours.

Another object of the present invention is to provide a multilayer nonwoven material, wherein said one
5 or more other layers which do not come into contact with the skin comprise a natural, synthetic, or semisynthetic material which acts as a reinforcement and/or a fluid absorption system for said multilayer nonwoven material, thus reducing the quantity of biocompatible and
10 bioabsorbable polymers to a minimum, concentrating their action in the area where it is needed.

A further object of the present invention is to provide a multilayer nonwoven material as above, wherein said surface layer which comes into contact with the
15 skin and said one or more other layers which do not come into contact with the skin are fixed together by at least one member selected from the group consisting of a coagulating chemical agent, an adhesive agent, and mechanical stitches.

20 Such multilayer nonwoven materials can be used, for example, as non-adhesive sanitary or surgical articles in surgery, in dermatology such as in treating skin pathologies, in odontostomatology, in orthopaedics, in neurosurgery, and in treating the ear or nose.

25 Further scope of the applicability of the present invention will become apparent from the detailed description provided below. However, it should be understood that the detailed description and specific examples, while indicating preferred embodiments of the
30 present invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the present invention will become apparent to those skilled in the art from this detailed description.

35 DETAILED DESCRIPTION OF THE INVENTION

The following detailed description of the invention

is provided to aid those skilled in the art in practicing the present invention. However, the following detailed description should not be construed to unduly limit the present invention, as modifications and variations in the embodiments discussed herein may be made by those of ordinary skill in the art without departing from the spirit or scope of the present inventive discovery.

The contents of each of the references cited herein are herein incorporated by reference in their entirety.

The foregoing and other objects are achieved by multilayer nonwoven tissues according to the present invention, with a basis weight of between 20 g/mq and 500 g/mq, a thickness of 0.5 mm to 20 mm, a minimum of 2 to 4 layers, a water absorption percentage compared to their weight of between 60% and 150%, and a water vapour permeability of between 100 and 4500 g/mq in 24 hrs.

The multilayer nonwoven tissue can be described as a material comprising several layers, fixed together by coagulating chemical agents and/or adhesive agents or by mechanical stitching methods. Each layer comprises fibers having a diameter varying between 8 and 60 micrometers and a length of between 5 mm and 100mm, joined together with coagulating chemical agents or adhesive agents, or by means of mechanical stitches.

The layer which is to come into contact with the skin is comprised of esters of hyaluronic acid such as those described in EPA 0 216 453 and U.S. Patents 4,851,521, 4,965,353, and 5,202,431, used either singly or in mixtures in varying percentages. Moreover, this layer can also comprise mixtures of fibers of hyaluronic acid esters with fibers obtained from natural polymers such as collagen or collagen and glycosaminoglycan coprecipitates, cellulose, polysaccharides in the form of gels such as chitin, chitosan, pectin, or pectic acid, agar, agarose, xanthan gum, gellan, alginic acid, various alginates, alginic acid esters, polymannan or

polyglycan, starches, natural gums, or fibers obtained from semisynthetic derivatives of natural polymers such as collagen cross-linked with cross-linking agents such as aldehydes or precursors of the same, dicarboxylic acids or halogenides of the same, diamines, derivatives of cellulose, alginic acid, starch, hyaluronic acid, chitin, chitosan, gellan, xanthan, pectin, pectic acids, polyglycan, polymannan, agar, agarose, natural gums, glycosaminoglycan, or with fibers obtained from synthetic polymers such as polylactic acid, polyglycolic acid or copolymers of the same or their derivatives, polydioxane, polyphosphazene, polysulfone, and polyurethane.

As employed herein, the term "derivative" refers to a compound containing the indicated moiety. For example, the term "cellulose derivative" denotes a compound containing a cellulose moiety.

The upper layers, which have the function of reinforcing the products and/or absorbing fluids and modulating the permeability to water vapours, may be in the form of nonwoven tissues or loom-woven structures. They may be constructed of natural fibers such as cotton, regenerated fibers such as viscose rayon, or fibers of synthetic polymers such as polyesters, polyamides, polyalkylenes, or mixtures thereof. Moreover, the layers can be composed of flexible foams, like polyurethane, or synthetic, elastomeric-type membranes such as elastomeric silicone or elastomeric polyurethane.

The various layers are fixed together by processes typical of nonwoven tissue techniques. These include, for example, mechanical stitching processes or chemical processes employing coagulating or adhesive agents, suitable for consolidating layers of fibers or for joining layers of various kinds, as described in Nonwoven Technologies for Sanitary Absorbent Products, pages 185-190. An exemplary

adhesive agent is an acrylic ester binder, Acronal DS 2331 X.

The present invention therefore relates to a new class of product, multilayer nonwoven tissues, for use
5 in the medical/pharmaceutical field to cover the skin and in surgery. The surface which comes into contact with the skin is composed of at least one hyaluronic acid ester used as such or in admixture with other natural or synthetic polymers; other layers of
10 synthetic or semisynthetic materials act as reinforcements of the material and/or fluid absorption systems.

The surface layer which comes into contact with the skin can also be comprised of a natural,
15 synthetic, or semisynthetic biocompatible perforated membrane compatible with cell growth on its surface. Examples of such natural and semisynthetic biocompatible perforated membranes are described in EP Application 0 462 426. Natural materials useful in
20 such membranes include collagen or coprecipitates of collagen and glycosaminoglycans, cellulose, gelled polysaccharides such as chitin, chitosan, pectins, pectic acids, agar, agarose, xanthan gum, gellan, alginic acid, alginates, polymannans, polyglucans,
25 starches, or natural rubbers, either alone or in mixture with each other or with polymers of synthetic or semisynthetic origin, in the presence of suitable precipitating or gelling agents such as metal salts, polycations, or polyanions. Examples of synthetic
30 biocompatible perforated membranes useful in the present multilayer nonwoven tissue include polylactic acid, polyglycolic acid, copolymers thereof or their derivatives, polydioxanones, polyphosphazenes, polysulfones, polyurethanes, semisynthetic derivatives
35 of natural polymers such as collagen crosslinked with crosslinking agents such as dialdehydes or their precursors, dicarboxylic acids or halides thereof,

diamines, or derivatives of cellulose, alginic acid, starch, chitin, chitosan, gellan, xanthan gum, pectins, pectic acids, polyglucans, polymannans, agar, agarose, natural rubbers, or glycosaminoglycans. Such
5 synthetic membranes can also comprise non-biodegradable synthetic polymers such as silicone, silane, or siloxane rubbers, fluoropolymers such as polyfluoroethylene, polyfluoropropylene, polyfluoroethers, polystyrene, vinyl polychloride,
10 polyacrylate or derivatives thereof, polyhydroxyacrylate, polyhydroxymethacrylate, carboxyvinyl polymers and their derivatives, maleic anhydride polymers and their derivatives, polyvinylchloride, polyvinylalcohol and its
15 derivatives, polyethylene, and polypropylene.

The nonwoven tissues of the present invention can also be impregnated with solutions of antibiotics, antiseptics, antimicrotocs, polypeptides, proteins, or any other type of pharmaceutically active compounds.

20 The characteristics of the new materials of the present invention make them especially valuable for use in the field of surgery, such as in otological and otoneurological microsurgery, functional, post-trauma and endoscopic rhino-sinusal microsurgery, plastic and
25 reconstructive surgery, and any other surgical indications involving the use of materials with the presently claimed characteristics, including their anti-adhesive properties.

For purely illustrative purposes, reported
30 hereafter are some examples of multilayer nonwoven tissues according to the present invention.

Example 1

A multilayer nonwoven tissue composed of a layer of hyaluronic acid benzyl ester, HYAFF 11, and a layer of
35 nonwoven viscose (Jettex 2005 from ORSA), basis weight 80 g/mq, thickness 2 mm, and water absorption percentage

560% by weight, was obtained by the following procedure.

The layer which comes into contact with the skin comprises fibers of HYAFF 11 produced by the wet-spinning technique in the form of a 30 g/mq sheet.

5 Fibers were made into sheets as described in WO 93/11803.

This layer is joined by stitching to a second layer of nonwoven viscose tissue with a basis weight of 30 g/mq.

10 The final nonwoven product thus comprises two perfectly adhered layers with a total basis weight of 80 g/mq, a thickness of 2 mm, and a water absorption percentage of 560% by weight.

Example 2

15 A multilayer nonwoven tissue comprising a layer of hyaluronic acid ethyl ester, HYAFF 7, and a layer of nonwoven polyester (BEST BOND 20 PS from FNT), with a basis weight of 50 g/mq, a thickness of 1 mm, and a water absorption of 400% by weight, is obtained
20 according to the following procedure.

The layer which comes into contact with the skin comprises fibers of HYAFF 7 produced by the wet-spinning technique in a 30-g/mq sheet which is joined by stitching to a second layer of nonwoven polyester with
25 a basis weight of 20 g/mq.

The final nonwoven product is thus composed of two perfectly adhered layers with a total basis weight of 50 g/mq, a thickness of 1 mm, and a water absorption percentage of 400% by weight.

Example 3

30 A multilayer nonwoven tissue comprising a mixed layer of hyaluronic acid benzyl ester, HYAFF 11, and calcium alginate in a 1:1 ratio and a reinforcing nonwoven tissue of polypropylene (spunbonded nonwoven
35 base, 50 g/mq from NEUBERGER) with a basis weight of

70 g/mq, a thickness of 1.5 mm, and a water absorption percentage of 450% by weight, was obtained by the following procedure.

5 Fibers of HYAFF 11 and calcium alginate, 40 mm in length, obtained by conventional wet-spinning techniques, were mixed, made into a 20 g/mq sheet, and joined by stitching to a spunbonded nonwoven tissue with a basis weight of 50 g/mq.

10 The resulting material comprises two layers of nonwoven tissue with a total basis weight of 70 g/mq, a thickness of 1.5 mm, and a water absorption percentage of 450% by weight.

Example 4

15 A multilayer nonwoven tissue comprising a layer of the 75% partial benzyl ester of hyaluronic acid, HYAFF 11p75, and a layer of polyurethane foam such as LYOBEND (from DELCON) with a basis weight of 100 g/mq, a thickness of 5 mm, and a water absorption percentage of 950% by weight, was obtained by the following
20 procedure.

 The layer which comes into contact with the skin comprises fibers of HYAFF 11p75 produced by the wet-spinning technique made into a 45 g/mq sheet and joined by stitching to a second layer of polyurethane
25 foam.

 The resulting nonwoven product comprises two layers perfectly joined together, with a total basis weight of 100 g/mq, a thickness of 4 mm, and a water absorption percentage of 950% by weight.

Example 5

30 A multilayer nonwoven tissue comprising a layer of hyaluronic acid benzyl ester HYAFF 11 and a layer of polyurethane foam such as LYOBEND (from DELCON) with a basis weight of 100 g/mq, a thickness of 6 mm,
35 and a water absorption percentage of 860% by weight,

was obtained by the following procedure.

The layer which comes into contact with the skin comprises fibers of HYAFF 11 produced by the wet-spinning technique and made into a 45 g/mq sheet which is joined by stitching to a second layer of polyurethane foam.

The resulting nonwoven product comprises two perfectly adhered layers with a total basis weight of 100 g/mq, a thickness of 6 mm, and a water absorption percentage of 860% by weight.

Example 6

A multilayer nonwoven tissue comprising three layers, with a basis weight of 200 g/mq and a thickness of 3 mm, wherein the layer coming into contact with the skin comprises a mixture of the partial benzyl ester of hyaluronic acid, HYAFF 11p75, and the benzyl ester of alginic acid, ALAFF 11, in equal proportions, a second layer comprising a cushion of polyurethane foam such as DS 50 FOAM (from ORSA) with a density of 55/69 Kg/cc (UNI regulation 6349), and a third layer comprising a polyurethane membrane with a water vapour permeability of 426 g/mq in 24 hours, was obtained according to the following procedure. The preparation of ALAFF 11 and other total and partial esters of alginic acid is described in EPA 0 251 905 and U.S. Patent 5,264,422.

Fibers of HYAFF 11 and ALAFF 11, 40 mm in length, obtained by a wet-spinning process, were stitched to the surface of the polyurethane foam cushion while the other surface was adhered with DURO-TAK 380-1054 glue (from NATIONAL) to the polyurethane membrane. The final material comprised three layers with a final basis weight of 200 g/mq, a thickness of 8 mm, a water absorption percentage of 1100% by weight, and a vapour permeability value of 450 g/mq in 24 hours.

Example 7

A multilayer nonwoven tissue comprising a layer of hyaluronic acid benzyl ester, HYAFF 11, and a layer of nonwoven viscose (Jettex 2005 from ORSA) with a basis weight of 80 g/mq and a thickness of 2 mm, joined to a HYAFF 11 membrane perforated with 0.5 mm holes produced as described in European Patent Application No. 0 462 426, was obtained according to the following procedure.

10 The HYAFF 11 surface of a nonwoven tissue obtained as described in Example 1 is sprayed with a solution of HYAFF 11/DMSO at a concentration of 60 mg/ml, after which a perforated membrane with 0.5 mm holes is applied to it. The membrane and nonwoven
15 tissue are then pressed together, immersed in an ethanol bath, washed, and dried.

The nonwoven tissue thus obtained has a basis weight of 80 g/mq, a thickness of 2 mm, and comprises three layers, one of which is formed by a perforated
20 membrane with 0.5 mm holes.

The invention being thus described, it is clear that the same can be modified in various ways. Such modifications are not to be considered as divergences from the spirit and purposes of the
25 present invention, and any modification which would appear evident to an expert in the art comes within the scope of the following claims.

CLAIMS:

1 1. A multilayer nonwoven material, comprising a
2 surface layer which comes into contact with the skin,
3 and one or more other layers which do not come into
4 contact with the skin, wherein said surface layer
5 which comes into contact with the skin is a member
6 selected from the group consisting of a surface layer
7 comprising at least one derivative of hyaluronic acid,
8 a surface layer comprising a mixture of said at least
9 one derivative of hyaluronic acid and at least one
10 natural polymer, semisynthetic polymer, or synthetic
11 polymer, and a surface layer comprising a natural,
12 synthetic, or semisynthetic biocompatible perforated
13 membrane compatible with cell growth on its surface.

1 2. A multilayer nonwoven material according to
2 claim 1, wherein said at least one derivative of
3 hyaluronic acid is a hyaluronic acid ester.

1 3. A multilayer nonwoven material according to
2 claim 1, wherein said at least one natural polymer is
3 a member selected from the group consisting of
4 collagen, a collagen-glycosaminoglycan coprecipitate,
5 cellulose, chitin, chitosan, pectin, pectic acid,
6 agar, agarose, xanthan gum, gellan, alginic acid, an
7 alginate, a polymanan, a polyglycan, a starch, and a

8 natural gum; said at least one semisynthetic polymer .
9 is a member selected from the group consisting of an
10 alginic acid ester, cross-linked collagen, a cellulose
11 derivative, an alginic acid derivative, a starch
12 derivative, a hyaluronic acid derivative, a chitin
13 derivative, a chitosan derivative, a gellan
14 derivative, a xanthan derivative, a pectin derivative,
15 a pectic acid derivative, a polyglycan derivative, a
16 polymannan derivative, an agar derivative, an agarose
17 derivative, a derivative of a natural gum, and a
18 glycosaminoglycan derivative; and said at least one
19 synthetic polymer is a member selected from the group
20 consisting of polylactic acid, polyglycolic acid, a
21 copolymer of polylactic acid and polyglycolic acid, a
22 copolymer of a derivative of polylactic acid and a
23 derivative of polyglycolic acid, a polydioxane, a
24 polyphosphazene, a polysulfone, and a polyurethane.

1 4. A multilayer nonwoven material according to
2 claim 1, wherein said one or more other layers which
3 do not come into contact with the skin comprise a
4 natural, synthetic, or semisynthetic material which
5 acts as a reinforcement and/or a fluid absorption
6 system for said multilayer nonwoven material.

1 5. A multilayer nonwoven material according to
2 claim 4, wherein said natural material is cotton, said
3 synthetic material is a member selected from the group
4 consisting of viscose rayon, a polyester, a polyamide,
5 a polyalkylene, a mixture of any of the foregoing, a
6 polyurethane, elastomeric silicone, and elastomeric
7 polyurethane, and said semisynthetic material is at
8 least one hyaluronic acid ester.

1 6. A multilayer nonwoven material according to
2 claim 1, wherein said surface layer which comes into
3 contact with the skin comprises at least one

4 hyaluronic acid ester.

1 7. A multilayer nonwoven material according to
2 claim 6, wherein said at least one hyaluronic acid
3 ester is a member selected from the group consisting
4 of a benzyl ester of hyaluronic acid and an ethyl
5 ester of hyaluronic acid.

1 8. A multilayer nonwoven material according to
2 claim 7, wherein said benzyl ester of hyaluronic acid
3 is a 75% partial benzyl ester of hyaluronic acid.

1 9. A multilayer nonwoven material according to
2 claim 1, wherein said surface layer which comes into
3 contact with the skin comprises a mixture of a
4 hyaluronic acid benzyl ester and an alginic acid
5 benzyl ester.

1 10. A multilayer nonwoven material according to
2 claim 1, wherein said surface layer which comes into
3 contact with the skin comprises a mixture of a
4 hyaluronic acid benzyl ester and calcium alginate.

1 11. A multilayer nonwoven material according to
2 claim 1, wherein said surface layer which comes into
3 contact with the skin comprises a natural, synthetic,
4 or semisynthetic biocompatible perforated membrane
5 which is compatible with cell growth on its surface.

1 12. A multilayer nonwoven material according to
2 claim 11, wherein said natural, synthetic, or
3 semisynthetic biocompatible perforated membrane has a
4 thickness of between 10 and 500 μ and possesses a
5 regular series of holes with a definite and constant
6 calibre of between 10 and 1000 μ , wherein each hole is
7 separated from its neighbor by a distance of between
8 50 and 1000 μ .

1 13. A multilayer nonwoven material according to
2 claim 11, wherein said semisynthetic biocompatible
3 perforated membrane comprises at least one hyaluronic
4 acid ester.

1 14. A multilayer nonwoven material according to
2 claim 13, wherein said at least one hyaluronic acid
3 ester is a hyaluronic acid benzyl ester.

1 15. A multilayer nonwoven material according to
2 claim 11, wherein said natural biocompatible
3 perforated membrane comprises a material selected from
4 the group consisting of collagen, a coprecipitate of
5 collagen and a glycosaminoglycan, cellulose, chitin,
6 chitosan, a pectin, a pectic acid, agar, agarose,
7 xanthan gum, gellan, alginic acid, an alginate, a
8 polymannan, a polyglucan, a starch, a natural rubber,
9 a mixture of any of the foregoing, a mixture of any of
10 the foregoing with a synthetic polymer, and a mixture
11 of any of the foregoing with a semisynthetic polymer.

1 16. A multilayer nonwoven material according to
2 claim 11, wherein said synthetic biocompatible
3 perforated membrane comprises a material selected from
4 the group consisting of polylactic acid, polyglycolic
5 acid, a copolymer of polylactic acid and polyglycolic
6 acid, a copolymer of a derivative of polylactic acid
7 and a derivative of polyglycolic acid, a
8 polydioxanone, a polyphosphazene, a polysulfone, a
9 polyurethane, a semisynthetic derivative of a natural
10 polymer, a cellulose derivative, alginic acid, starch,
11 chitin, chitosan, gellan, xanthan gum, a pectin, a
12 pectic acid, a polyglucan, a polymannan, agar,
13 agarose, a natural rubber, a glycosaminoglycan,
14 silicone, silane, a siloxane rubber, a fluoropolymer,
15 polystyrene, vinyl polychloride, polyacrylate, a
16 derivative of polyacrylate, polyhydroxyacrylate,

17 polyhydroxymethacrylate, a carboxyvinyl polymer, a
18 carboxyvinyl polymer derivative, a maleic anhydride
19 polymer, a maleic anhydride polymer derivative,
20 polyvinylchloride, polyvinylalcohol, a
21 polyvinylalcohol derivative, polyethylene, and
22 polypropylene.

1 17. A multilayer nonwoven material according to
2 claim 16, wherein said semisynthetic derivative of a
3 natural polymer is collagen crosslinked with a
4 crosslinking agent selected from the group consisting
5 of a dialdehyde, a dialdehyde precursor, a
6 dicarboxylic acid, a halide of a dicarboxylic acid,
7 and a diamine.

1 18. A multilayer nonwoven material according to
2 claim 16, wherein said fluoropolymer is a material
3 selected from the group consisting of
4 polyfluoroethylene, polyfluoropropylene, and a
5 polyfluoroether.

1 19. A multilayer nonwoven material according to
2 claim 1, wherein said one or more other layers which
3 do not come into contact with the skin comprise
4 viscose.

1 20. A multilayer nonwoven material according to
2 claim 1, wherein said one or more other layers which
3 do not come into contact with the skin comprise
4 nonwoven spunbonded polypropylene.

1 21. A multilayer nonwoven material according to
2 claim 1, wherein said one or more other layers which
3 do not come into contact with the skin comprise a
4 polyurethane foam.

1 22. A multilayer nonwoven material according to

2 claim 1, having a basis weight of between 40 g/mq and
3 500 g/mq, a thickness of between 0.5 mm and 20 mm, a
4 fiber diameter of between 8 μ m and 60 μ m, a length of
5 between 5 mm and 100 mm, 2 to 4 layers, a water
6 absorption percentage of 60% to 500%, and a water
7 vapour permeability value of between 100 and 4500 g/mq
8 in 24 hours.

1 23. A multilayer nonwoven material according to
2 claim 1, wherein said surface layer which comes into
3 contact with the skin and said one or more other layers
4 which do not come into contact with the skin are fixed
5 together by at least one member selected from the group
6 consisting of a coagulating chemical agent, an adhesive
7 agent, and mechanical stitches.

1 24. A multilayer nonwoven material according to
2 claim 1, comprising two or more layers stitched
3 together.

1 25. A multilayer nonwoven material according to
2 claim 1, comprising two layers stitched together,
3 wherein said layer which does not come into contact
4 with the skin comprises a polyurethane foam.

1 26. A multilayer nonwoven material according to
2 claim 1, comprising three layers, wherein said layer
3 which comes into contact with the skin is a
4 biocompatible perforated membrane comprising a total
5 benzyl ester of hyaluronic acid.

1 27. A multilayer nonwoven material according to
2 claim 1, containing a pharmaceutically active compound.

1 28. A multilayer nonwoven material according to
2 claim 27, wherein said pharmaceutically active compound
3 is a member selected from the group consisting of an

4 antibiotic, an antiseptic, an antimetabolic, a poly-
5 peptide, and a protein.

1 29. Use of said multilayer nonwoven material
2 according to any one of claims 1 to 28 in surgery.

1 30. Use of said multilayer nonwoven material
2 according to any one of claims 1 to 28 to treat skin
3 pathologies.

1 31. Use of said multilayer nonwoven material
2 according to any one of claims 1 to 28 in dermatology.

1 32. Use of said multilayer nonwoven material
2 according to any one of claims 1 to 28 in
3 odontostomatology.

1 33. Use of said multilayer nonwoven material
2 according to any one of claims 1 to 28 in orthopaedics.

1 34. Use of said multilayer nonwoven material
2 according to any one of claims 1 to 28 in neurosurgery.

1 35. Use of said multilayer nonwoven material
2 according to any one of claims 1 to 28 in treating the
3 ear or nose.

1 36. Use of said multilayer nonwoven material
2 according to any one of claims 1 to 28 as an anti-
3 adhesive material.

INTERNATIONAL SEARCH REPORT

Int. Application No
PCT/EP 94/00397

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A61L15/28 A61L15/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A61L C08B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP,A,0 462 426 (FIDIA S.P.A.) 27 December 1991 cited in the application see page 3, line 31 - line 41; examples ---	1-36
P,Y	WO,A,93 11803 (M.U.R.S.T.) 24 June 1993 cited in the application see claims; examples ---	1-36
P,Y	WO,A,94 01468 (M.U.R.S.T.) 20 January 1994 see claims; examples ---	1-36
A	EP,A,0 216 453 (FIDIA S.P.A.) 1 April 1986 cited in the application see examples --- -/--	1-36

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

24 May 1994

Date of mailing of the international search report

06.05.94

Name and mailing address of the ISA

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Authorized officer

ESPINOSA, M

INTERNATIONAL SEARCH REPORT

Int :onal Application No
PCT/EP 94/00397

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP,A,0 341 745 (FIDIA S.P.A.) 15 November 1989 see claims; examples -----	1

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 94/00397

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 29-36 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 94/00397

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0462426	27-12-91	AU-B- 637235 AU-A- 7806691 CA-A- 2043527 JP-A- 4231061	20-05-93 05-12-91 02-12-91 19-08-92
WO-A-9311803	24-06-93	AU-B- 3346693	19-07-93
WO-A-9401468	20-01-94	NONE	
EP-A-0216453	01-04-87	AU-B- 591501 AU-A- 5983686 JP-A- 62064802 US-A- 4965353 US-A- 5202431 US-A- 4851521	07-12-89 26-02-87 23-03-87 23-10-90 13-04-93 25-07-89
EP-A-0341745	15-11-89	AU-B- 631125 AU-A- 3574789 WO-A- 8910941 JP-T- 2504163	19-11-92 29-11-89 16-11-89 29-11-90